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10/583,805

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Muthukumaran Natarajan

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MERCHANT & GOULD PC
P.O. BOX 2903
MINNEAPOLIS, MN 55402-0903

EXAMINER

LOEWE, SUN JAE Y

ART UNIT

PAPER NUMBER

1626

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|--------------------------------------|---|--|
| Office Action Summary | Application No. 10/583,805 | Applicant(s) NATARAJAN ET AL. | |
| | Examiner SUN JAE Y. LOEWE | Art Unit 1626 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 July 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4,9-12 and 16 is/are pending in the application.
- 4a) Of the above claim(s) 9-12 and 16 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>8-25-2006</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 1-4, 9-12 and 16 are pending in the instant application.

Election/Restrictions

2. Applicant's election with traverse of Group I, and species of polymorph IV, in the reply filed on July 2, 2008 is acknowledged. The traversal is on the ground(s):

“ Applicants have amended the claims so both the product claims and the process claims only recite polymorph IV of tiagabine hydrochloride. Applicants respectfully assert that the instant Group II claims (now claims 9-12 and 16 following amendment, which only recite polymorph IV of tiagabine hydrochloride) should be rejoined and examined in the same application. ”

The argument has been considered, however, it is not found to be persuasive. It is noted that the amended claims are still drawn to more than one species - ie. polymorph of tiagabine hydrochloride – in view of the reasons provided below.

The requirement is still deemed proper and is therefore made FINAL.

3. Pursuant MPEP 1893.03

“(Excerpts)

Once the national stage application has been taken up by the examiner, prosecution proceeds in the same manner as for a domestic application with the exceptions that:

(A) the international filing date >(or, if appropriate, the priority date)< is the date to keep in mind when searching the prior art; and

(B) unity of invention proceeds as under 37 CFR 1.475.

.....

¶ 18.20 National Stage Election of Species in 35 U.S.C.

371 Applications

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows:

[1]

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(s). ”

the search and examination detailed in this office action was performed following the guidelines provided by MPEP 803.02

“(Excerpts)”

Markush-type claim will be examined fully with respect to the elected species and further to the extent necessary to determine patentability. If the Markush-type claim is not allowable **, the provisional election will be given effect and examination will be limited to the Markush-type claim and claims to the elected species, with claims drawn to species patentably distinct from the elected species held withdrawn from further consideration.

If on examination the elected species is found to be anticipated or rendered obvious by prior art, the Markush-type claim and claims to the elected species shall be rejected, and claims to the non-elected species would be held withdrawn from further consideration.”

The elected species (ie. polymorph IV of tiagabine hydrochloride which is the polymorphic form tiagabine hydrochloride exhibiting XRD pattern provided by claim 2 and unit cell parameters provided by claim 3) may not be novel over the prior art. Furthermore, the generic claims encompassing the elected species were not compliant with 35 USC 112 1st and 2nd paragraphs.

For these reasons, the provisional election was given effect and non-elected species were withdrawn from further consideration.

4. Claims 9-12 and 16 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected subject matter. Applicant timely traversed the election of species requirement in the response dated July 2, 2008.

Priority

5. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

6. The information disclosure statement (IDS) submitted on August 25, 2006 was in compliance with the provisions of 37 CFR 1.97 and 37 CFR 1.98. The IDS was considered. A signed copy of form 1449 is enclosed herewith.

Claim Objections

7. Claims 1-4 objected to for containing non-elected subject matter. The non-elected subject matter consists of species that are not the election denoted above. Applicant will be entitled to rejoinder of non-elected species upon allowability of the generic claims.

Specification

8. The disclosure is objected to because it is missing a section entitled "Brief Description of Drawings" (MPEP 608.01(f) and 37 CFR 1.74). Appropriate correction is required.

Claim Rejections - 35 USC § 112 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1 and 4 rejected under 35 U.S.C 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The prior art provides a method of comparing X-ray powder diffraction data by overlaying and aligning the respective films or plots. The comparison of peak positions and intensities shows whether the crystalline forms are the same or different (Byrn et al., page 63). An X-ray diffraction pattern is a fingerprint that defines a polymorph; the presence and absence of peaks are both important factors in establishing such fingerprint.

The claims are drawn to a “stable polymorph IV of tiagabine hydrochloride” identified by the x-ray diffraction (XRD) pattern of Figure 2. However, the claims recite merely a few selected peaks in the XRD pattern. The specification does not provide guidance or reasoning as to why such “abbreviated pattern” is sufficient to uniquely identify the claimed polymorph (eg. see also Section 12, below).

Therefore, the claims are drawn to subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

10. Claims 1 and 4 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the preparation of “polymorph IV of tiagabine hydrochloride” identified by the x-ray diffraction pattern shown in Figure 2, is not enabling for the preparation of other polymorphs of the claimed compound. Thus, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with the claims.

The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8USPQ2s 1400, 1404 (Fed. Cir. 1988). MPEP 2164.01(a) states “There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue”. The factors are applied below to the instant claims.

The breadth of the claims

The claims encompass polymorphs of tiagabine hydrochloride characterized by the presence of peaks set forth in claims 1 and 4

The nature of the invention

In view of the discussion above (Section 9), the claims as drafted, within the broadest reasonable interpretation, encompass more than one polymorph of tiagabine hydrochloride.

The state of the prior art/level of ordinary skill/level of predictability

The state of the art for preparing polymorphs of a given compound is unpredictable (eg. see Chawla et al., p. 9, 1st and 2nd paragraphs):

- The number or existence of solid forms cannot be predicted.

Art Unit: 1626

- The more diligently any system is studied the larger the number of polymorphs *discovered*
- It is not commonly known in the art, or predictable, how different solid forms are made (Newman et al., p. 898, 2nd column, last paragraph).

The amount of direction provided by the inventor/existence of working examples

Direction/working examples limited to the preparation of a polymorph of tiagabine hydrochloride characterized by the XRD pattern provided by Figure 2.

The quantity of experimentation needed to make or use the invention

MPEP 2164.01(a) states:

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to:

- (A) The breadth of the claims;
- (B) The nature of the invention;
- (C) The state of the prior art;
- (D) The level of one of ordinary skill;
- (E) The level of predictability in the art;
- (F) The amount of direction provided by the inventor;
- (G) The existence of working examples; and
- (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Based on the evidence regarding each of the above factors (see discussion above), the specification, at the time the application was filed, would not have taught one of ordinary skill in the art how to practice the claimed invention without undue experimentation.

The instant claims *prima facie* lack enablement.

Claim Rejections - 35 USC § 112 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 1-4 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims refer to “a stable polymorph ... having characteristic peaks... at about.”

“About” is a relative term which renders the claim indefinite; the term is not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

“Stable” is not defined by the claims or specification. It is not clear how this term limits the instant claims. Therefore, the metes and the bounds of the claims cannot be interpreted.

Appropriate correction of the issues described above is requested.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1, 3 and 4 rejected under 35 U.S.C. 102(b) or, in the alternative, under 35 U.S.C. 103(a) as obvious over Ahrndt et al. (US 5,958,951).

The reference teaches a polymorphic form of the claimed compound having the same peaks as set forth in the claim 1. See Figure 8, bottom XRD pattern. The reference does not teach the unit cell parameters or particle size of the disclosed polymorph. Thus, the difference

Art Unit: 1626

between the prior art polymorph and the instantly claimed form lies on characteristics (unit cell parameters and particle size) for which the reference happens to be silent. This is not an ordinary inherency situation, however, as stated in *Ex parte Anderson*, 21 USPQ 2nd 1241 and 1251 “There is ample precedent for shifting the burden to an applicant to reproduce a prior art product whose final structure or properties are, at least, in part determined by the precise process used in its manufacture.” (page 1253). Furthermore, MPEP 2112.V states that “once a reference teaching product appearing to be substantially identical is made the basis of a rejection, and the examiner presents evidence or reasoning tending to show inherency, the burden shifts to the applicant to show an unobvious difference.

To overcome this rejection, Applicant is requested to provide a showing of how the instantly claimed crystalline form is different (or unobvious) from the polymorph disclosed by the reference.

13. Claims 1-4 rejected under 35 U.S.C. 102(b) or, in the alternative, under 35 U.S.C. 103(a) as obvious over Andersen et al. (J. Med. Chem., pg. 1717 and 1722 2nd column).

The reference teaches a solid form of the claimed compound which is obtained by crystallization of the product from acetone. The reference does not teach a specific polymorph, because the inherent feature that defines such form (eg. XRD data) is not disclosed. Thus, the difference between the prior art solid and the instantly claimed crystalline form lies on characteristics (XRD pattern) for which the reference happens to be silent. This is not an ordinary inherency situation, however, as stated in *Ex parte Anderson*, 21 USPQ 2nd 1241 and 1251 “There is ample precedent for shifting the burden to an applicant to reproduce a prior art product whose final structure or properties are, at least, in part determined by the precise process

used in its manufacture.” (page 1253). Furthermore, MPEP 2112.V states that “once a reference teaching product appearing to be substantially identical is made the basis of a rejection, and the examiner presents evidence or reasoning tending to show inherency, the burden shifts to the applicant to show an unobvious difference.

To overcome this rejection, Applicant is requested to provide a showing of how the instantly claimed crystalline form is different from the solid form disclosed by the reference.

14. Claims 1-4 rejected under 35 U.S.C. 102(b) or, in the alternative, under 35 U.S.C. 103(a) as obvious over Gronvald et al. (US 5,010,090).

The reference teaches a solid form of the claimed compound which is isolated from ethyl acetate (see columns 9 and 10). The reference does not teach a specific polymorph, because the inherent feature that defines such form (eg. XRD data) is not disclosed. Thus, the difference between the prior art solid and the instantly claimed crystalline form lies on characteristics (XRD pattern) for which the reference happens to be silent. This is not an ordinary inherency situation, however, as stated in *Ex parte Anderson*, 21 USPQ 2nd 1241 and 1251 “There is ample precedent for shifting the burden to an applicant to reproduce a prior art product whose final structure or properties are, at least, in part determined by the precise process used in its manufacture.” (page 1253). Furthermore, MPEP 2112.V states that “once a reference teaching product appearing to be substantially identical is made the basis of a rejection, and the examiner presents evidence or reasoning tending to show inherency, the burden shifts to the applicant to show an unobvious difference.

To overcome this rejection, Applicant is requested to provide a showing of how the instantly claimed crystalline form is different from the solid form disclosed by the reference.

Conclusion

15. No claims allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUN JAE Y. LOEWE whose telephone number is (571)272-9074. The examiner can normally be reached on M-F 7:30-5:00 Est.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571)272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sun Jae Y. Loewe, Ph.D./
8-18-2008

/Kamal A Saeed, Ph.D./
Primary Examiner, Art Unit 1626